



PAPAIN

This monograph is intended to serve as a guide to industry for the preparation of Product Licence Applications (PLAs) and labels for natural health product market authorization. It is not intended to be a comprehensive review of the medicinal ingredient.

Notes

- ▶ Text in parentheses is additional optional information which can be included on the PLA and product label at the applicant's discretion.
- ▶ The solidus (/) indicates that the terms and/or the statements are synonymous. Either term or statement may be selected by the applicant.

Date

July 10, 2012

Proper name(s)

Papain (IUBMB 2000)

Common name(s)

Papain (IUBMB 2000)

Source material(s)

- ▶ Fruit of papaya (*Carica papaya* L. (Caricaceae)) (Merck 2012; USDA 2011; Morton 1987)
- ▶ Leaf of papaya (*Carica papaya* L. (Caricaceae)) (Merck 2012; USDA 2011; Morton 1987)

Route(s) of administration

Oral

Dosage form(s)

- ▶ The acceptable pharmaceutical dosage forms include, but are not limited to capsules, chewables (e.g. gummies, tablets), liquids, powders, strips or tablets.
- ▶ This monograph is not intended to include foods or food-like dosage forms such as bars, chewing gums or beverages.

Use(s) or Purpose(s) Statement(s) to the effect of:

Digestive enzyme (Merck 2012)

Dose(s)

Subpopulation(s)

Adults (≥ 19 years)

Quantity(ies)

Dose information must include the quantities of both the enzyme preparation and its enzymatic activity:

- ▶ Providing up to 1.2×10^3 mg per day enzyme preparation of the latex from the leaf and/or unripe fruit of papaya; not to exceed 400 mg per dose (Dörr and Herrman 2007; Martin et al. 2002; Dale et al. 2001; Morton 1987); and
- ▶ Enzyme activity providing up to 7.2×10^6 FCC PU per day; not to exceed 2.4×10^6 FCC PU per dose (Martin et al. 2002; Dale et al. 2001).

Notes

- ▶ One papain unit (PU) is defined as that quantity of enzyme that liberates the equivalent of 1 μ g of tyrosine per hour under the conditions of the assay (FCC 8).
- ▶ One FCC papain unit is approximately equivalent to one USP papain unit (1 FCC PU \approx 1 USP PU).
- ▶ For multi-ingredient products containing both papain and bromelain (fruit and/or stem), the combined proteolytic activity should not exceed the maximum proteolytic activity of 1.3×10^8 FCC PU per day (as per the NHPD *Bromelain, Stem* monograph).

Directions for use

Take with food/a meal.

Duration of use

For prolonged use, consult a health care practitioner.

Risk information Statement(s) to the effect of:

Caution(s) and warning(s)

- ▶ If you are pregnant or breastfeeding, consult a health care practitioner prior to use.

- ▶ If you have a gastrointestinal lesion/ ulcer, are taking an anticoagulant/ blood thinner or an anti-inflammatory, or are having surgery, consult a health care practitioner prior to use (Martindale 2011).
- ▶ If you have allergy to latex or fruits (such as avocado, banana, chestnut, passion fruit, fig, melon, mango, kiwi, pineapple, peach, and tomato), consult a health care practitioner prior to use (US FDA 2008; APhA 2006; Brehler et al. 1997).

Contraindication(s)

No statement required.

Known adverse reaction(s)

Hypersensitivity/allergy has been known to occur, in which case discontinue use (HC 2011; Martindale 2011; US FDA 2008).

Non-medicinal ingredients

Must be chosen from the current NHPD *Natural Health Products Ingredients Database* and must meet the limitations outlined in the database.

Specifications

- ▶ The finished product must comply with the minimum specifications outlined in the current NHPD *Compendium of Monographs*.
- ▶ Details of the manufacturing of the enzyme at the raw material stage should include fermentation medium and the isolation process of the medicinal ingredient.
- ▶ The specifications must include testing for enzymatic activity of the medicinal ingredient at appropriate stages of formulation and manufacturing using the assay outlined in the current Food Chemicals Codex (FCC):
PLANT PROTEOLYTIC ACTIVITY.
- ▶ The medicinal ingredient may comply with the specifications outlined in the current United States Pharmacopeia (USP):
Papain.
- ▶ Where published methods are not suitable for use, manufacturers will use due diligence to ensure that the enzymes remain active to the end of their shelf life indicated on the product label.

References cited

APhA 2006: Berardi RR, Kroon LA, McDermott JH, Newton GD, Oszko MA, Popovich NG, Remington TL, Rollins CJ, Shimp LA, Tietze KJ, editors. *Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care*. 15th edition. Washington (DC): APhA Publications; 2006.

Brehler R, Theissen U, Mohr C, Luger T. 1997. "Latex-fruit syndrome": frequency of cross-reacting IgE antibodies. *Allergy* 52(4):404-410.

Dale PS, Tamhankar CP, George D, Daftary GV. 2001. Co-medication with hydrolytic enzymes in radiation therapy of uterine cervix: evidence of the reduction of acute side effects. *Cancer Chemotherapy and Pharmacology* 47(Suppl):S29-S34.

Dörr W, Herrmann T. 2007. Efficacy of Wobe-Mugos® E for reduction of oral mucositis after radiotherapy. *Strahlentherapie und Onkologie* 183:121-127.

FCC 8: Food Chemicals Codex. Eighth edition. Rockville (MD): The United States Pharmacopeial Convention; 2012.

HC 2011: Canada Vigilance Adverse Reaction Online Database. Search Criteria: Papain. [Accessed 2012 March 16]. Available from:
<http://www.hc-sc.gc.ca/dhp-mps/medeff/databasdon/index-eng.php>

IUBMB 2000: Nomenclature Committee of the International Union of Biochemistry and Molecular Biology. [Internet]. London (GB): Queen Mary, University of London [papain: CAS 9001-73-4, EC 3.4.22.2 created 1961 as EC 3.4.4.10, transferred 1972 to EC 3.4.22.2, modified 1976, modified 2000; Accessed 2012 March 16]. Available from:
<http://www.chem.qmul.ac.uk/iubmb/enzyme/EC3/4/22/2.html>

Martin T, Uhder K, Kurek R, Roeddiger S, Schneider L, Vogt HG, Heyd R, Zamboglou N. 2002. Does prophylactic treatment with proteolytic enzymes reduce acute toxicity of adjuvant pelvic irradiation? Results of a double-blind randomized trial. *Radiotherapy and Oncology* 65:17-22.

Martindale 2011: Sweetman SC, editor. 2011. *Martindale: The Complete Drug Reference*. [Internet]. London (GB): Pharmaceutical Press. [Papain: CAS 9001-73-4, syn: EC 3.4.22.2, latest modification: 10-Oct-2011; Accessed 2012 July 9]. Available from:
<http://www.medicinescomplete.com>

Merck 2012: *The Merck Index Version 14.1* [Internet]. Whitehouse Station (NJ): Merck & Co., Inc. [published 2006, updated 2012; Accessed 2012 July 10]. Available from:
<http://www.medicinescomplete.com/mc/merck/current/monographs.htm>

Morton J. 1987. Papaya. In: Morton JF. *Fruits of Warm Climates*. Miami (FL): Julia F. Morton; p. 336–346. [Accessed 2012 March 16]. Available from:
http://www.hort.purdue.edu/newcrop/morton/papaya_ars.html

USDA 2011: United States Department of Agriculture, Agricultural Research Service, National Genetic Resources Program. Germplasm Resources Information Network (GRIN) [online database]. Beltsville (MD): National Germplasm Resources Laboratory. [*Carica papaya* L. (Caricaceae): Last updated 09-May-2011; Accessed 2012 March 16]. Available from:
http://www.ars-grin.gov/cgi-bin/npgs/html/tax_search.pl

US FDA 2008: Topical Drug Products Containing Papain; Enforcement Action Dates. Department of Health and Human Services. Docket No. FDA-2008-N-0481.

USP 35: United States Pharmacopeia and the National Formulary (USP 35 - NF 30). Rockville (MD): The United States Pharmacopeial Convention; 2012.

References reviewed

Repchinsky C, editor-in-chief. Patient Self-Care: Helping Patients Make Therapeutic Choices, 1st edition. Ottawa (ON): Canadian Pharmacists Association.